

10

15

20

5. The method of claim 4, wherein the antidepressant drug is administered about 0.25 to about 3.5 hours prior to sexual activity.

25

7. The method of claim 6, wherein the active agent is administered about 1 to about 2.5 hours prior to sexual activity.

30

8. The method of any one of claims 4, 5, 6 and 7, wherein the sexual activity is sexual intercourse.

9. The method of claim 2, wherein the formulation is an immediate release dosage form.

5           10. The method of claim 3, wherein the formulation is an immediate release unit dosage form.

11. The method of claim 1, wherein the active agent is administered orally.

10           12. The method of claim 11, wherein the pharmaceutical formulation is selected from the group consisting of tablets, capsules, caplets, solutions, suspensions syrups granules, beads, powders and pellets.

15           13. The method of claim 12, wherein the pharmaceutical formulation comprises a tablet.

14. The method of claim 12, wherein the pharmaceutical formulation comprises a capsule.

20           15. The method of claim 1, wherein the active agent is administered transmucosally.

16. The method of claim 15, wherein the active agent is administered sublingually.

25           17. The method of claim 15, wherein the active agent is administered buccally.

18. The method of claim 15, wherein the active agent is administered intranasally.

30

09596407 201905550  
PATENT

19. The method of claim 15, wherein the active agent is administered transurethrally.

20. The method of claim 15, wherein the active agent is administered rectally.

21. The method of claim 1, wherein the active agent is administered by inhalation.

22. The method of claim 1, wherein the active agent is administered transdermally.

23. The method of claim 1, wherein the active agent is administered parenterally.

24. The method of claim 1, wherein the antidepressant drug is selected from the group consisting of tricyclic antidepressants, tetracyclic antidepressant drugs, and combinations thereof.

25. The method of claim 24, wherein the antidepressant drug is selected from the group consisting of amitriptyline, amoxapine, butriptyline, clomipramine, demexiptiline, desipramine, dibenzepin, dimetacrine, dothiepin, doxepin, imipramine, iprindole, lofepramine, maprotiline, melitracen, metapramine, mianserin, mirtazapine, nortriptyline, propizepine, protriptyline, quinupramine, setiptiline, tianeptine, trimipramine, and combinations thereof.

26. The method of claim 25, wherein the antidepressant drug is clomipramine or an acid addition salt thereof.

27. The method of claim 26, wherein the antidepressant drug is clomipramine hydrochloride.

28. The method of claim 1, wherein the antidepressant drug is selected from the group consisting of monoamine oxidase inhibitors.

5           29. The method of claim 28, wherein the antidepressant drug is selected from the group consisting of amiflamine, brofaromine, clorgyline,  $\alpha$ -ethyltryptamine, iproclozide, iproniazid, isocarboxazid, mebanazine, moclobemide, nialamide, pargyline, phenelzine, pheniprazine, pirlindole, safrazine, selegiline, tolloxatone, tranylcypromine, and combinations thereof.

10           30. The method of claim 1, wherein the antidepressant drug is selected from the group consisting of azaspirone antidepressants.

15           31. The method of claim 30, wherein the antidepressant drug is selected from the group consisting of buspirone, gepirone, ipsapirone, tandospirone, tiaspirone, and combinations thereof.

20           32. The method of claim 1, wherein the antidepressant drug is an atypical non-SRI antidepressant selected from the group consisting of amesergide, amineptine, benactyzine, bupropion, fezolamine, levoprotiline, medifoxamine, mianserin, minaprine, oxaflozane, oxitriptan, rolipram, teniloxazine, tofenacin, trazodone, tryptophan, viloxazine, and combinations thereof.

25           33. The method of claim 1, further comprising administering at least one additional active agent with the antidepressant drug.

30           34. The method of claim 33, wherein the additional active agent is a vasoactive agent selected from the group consisting of nitroglycerin, isosorbide dinitrate, erythrityl tetranitrate, amyl nitrate, sodium nitroprusside, molsidomine, linsidomine chlorhydrate, S-nitroso-N-acetyl-d,l-penicillamine, S-nitroso-N-cysteine and S-nitroso-N-glutathione,

TOPTT 20496660

0996407-112101  
0496660

diazonium diolates ("NONOates"), phenoxybenzamine, dibenamine, doxazosin, terazosin, phentolamine, tolazoline, prazosin, trimazosin, alfuzosin, tamsulosin, indoramin, ergotamine, acetergamine, brazergoline, bromerguride, cianergoline, delorgotril, disulergine, ergonovine maleate, ergotamine tartrate, etisulergine, lergotril, lysergide, mesulergine, metergoline, metergotamine, nicergoline, pergolide, propisergide, proterguride, diazoxide, hydralazine, minoxidil nimodepine, pinacidil, cyclandelate, dipyridamole, isoxsuprine, chlorpromazine, haloperidol, yohimbine, prostaglandin E<sub>0</sub>, prostaglandin E<sub>1</sub>, prostaglandin A<sub>1</sub>, prostaglandin B<sub>1</sub>, prostaglandin F<sub>1α</sub>, 19-hydroxy-prostaglandin A<sub>1</sub>, 19-hydroxy- prostaglandin B<sub>1</sub>, prostaglandin E<sub>2</sub>, prostaglandin A<sub>2</sub>, prostaglandin B<sub>2</sub>, 19-hydroxy- prostaglandin A<sub>2</sub>, 19-hydroxy- prostaglandin B<sub>2</sub>, prostaglandin E<sub>3</sub>, prostaglandin F<sub>3α</sub>, carboprost tromethamine, dinoprost tromethamine, dinoprostone, lipoprost, gemeprost, metenoprost, sulprostone, tiaprost, vasoactive intestinal peptide, and combinations thereof.

15           35. The method of claim 33, wherein the additional active agent is a phosphodiesterase inhibitor.

          36. The method of claim 35, wherein the phosphodiesterase inhibitor is a Type III, Type IV, Type V, or nonspecific phosphodiesterase inhibitor.

20           37. The method of claim 33, wherein the additional active agent is selected from the group consisting of cianopramine, citalopram, femoxetine, fluoxetine, fluvoxamine, ifoxetine, milnacipran, nomifensine, oxaprotiline, paroxetine, sertraline, sibutramine, venlafaxine, viqualine, zimeldine, clovoxamine, etoperidone, methylphenidate, nefazodone, opipramol, 2-methyl serotonin, lysergic acid diethylamide, ergot alkaloids, 8-hydroxy-(2-N,N-dipropylamino)-tetraline, 1-(4-bromo-2,5-dimethoxyphenyl)-2-aminopropane, cisapride, sumatriptan, *m*-chlorophenylpiperazine, zacopride, mezacopride, ondansetron, granisetron, metoclopramide, tropisetron, dolasetron, trimethobenzamide, methysergide, risperidone, ketanserin, ritanserin, clozapine, R(+)-- (2,3-dimethoxyphenyl)-1-[2-(4-fluorophenyl)ethyl]-4-piperidine-methanol, azatadine,

25           38. The method of claim 33, wherein the additional active agent is selected from the group consisting of citalopram, fluoxetine, fluvoxamine, ifoxetine, milnacipran, nomifensine, oxaprotiline, paroxetine, sertraline, sibutramine, venlafaxine, viqualine, zimeldine, clovoxamine, etoperidone, methylphenidate, nefazodone, opipramol, 2-methyl serotonin, lysergic acid diethylamide, ergot alkaloids, 8-hydroxy-(2-N,N-dipropylamino)-tetraline, 1-(4-bromo-2,5-dimethoxyphenyl)-2-aminopropane, cisapride, sumatriptan, *m*-chlorophenylpiperazine, zacopride, mezacopride, ondansetron, granisetron, metoclopramide, tropisetron, dolasetron, trimethobenzamide, methysergide, risperidone, ketanserin, ritanserin, clozapine, R(+)-- (2,3-dimethoxyphenyl)-1-[2-(4-fluorophenyl)ethyl]-4-piperidine-methanol, azatadine,

30           39. The method of claim 33, wherein the additional active agent is selected from the group consisting of citalopram, fluoxetine, fluvoxamine, ifoxetine, milnacipran, nomifensine, oxaprotiline, paroxetine, sertraline, sibutramine, venlafaxine, viqualine, zimeldine, clovoxamine, etoperidone, methylphenidate, nefazodone, opipramol, 2-methyl serotonin, lysergic acid diethylamide, ergot alkaloids, 8-hydroxy-(2-N,N-dipropylamino)-tetraline, 1-(4-bromo-2,5-dimethoxyphenyl)-2-aminopropane, cisapride, sumatriptan, *m*-chlorophenylpiperazine, zacopride, mezacopride, ondansetron, granisetron, metoclopramide, tropisetron, dolasetron, trimethobenzamide, methysergide, risperidone, ketanserin, ritanserin, clozapine, R(+)-- (2,3-dimethoxyphenyl)-1-[2-(4-fluorophenyl)ethyl]-4-piperidine-methanol, azatadine,

0956407 442104  
F012T 2045550

cyproheptadine, fenclonine, dexfenfluramine, fenfluramine, chlorpromazine,  
methoxamine, methpentamine, metaraminol, mitodrine, clonidine, apraclonidine,  
guanfacine, guanabenz, methyldopa, amphetamine, methamphetamine, epinephrine,  
norepinephrine, ethylnorepinephrine, phenylephrine, ephedrine, pseudoephedrine,  
5 pemoline, naphazoline, tetrahydrozoline, oxymetazoline, xylometazoline,  
phenylpropanolamine, phenylethylamine, dopamine, dobutamine, colterol, isoproterenol,  
isotharine, metaproterenol, terbutaline, tyramine, hydroxyamphetamine, ritodrine,  
prenalterol, albuterol, isoetharine, pirbuterol, bitolterol, fenoterol, formoterol, procaterol,  
salmeterol, mephenterine, propylhexedrine, phenoxybenzamine, phentolamine,  
10 tolazoline, prazosin, terazosin, doxazosin, trimazosin, yohimbine, labetalol, urapidil,  
alfuzosin, bunazosin, tamsulosin, haloperidol, phenothiazines, butyrophenones,  
propranolol, nadolol, timolol, pindolol, metoprolol, atenolol, esmolol, acebutolol,  
bopindolol, carteolol, oxprenolol, penbutolol, carvedilol, medroxalol, naftopidil,  
bucindolol, levobunolol, metipranolol, bisoprolol, nebivolol, betaxolol, carteolol,  
15 celiprolol, sotalol, propafenone, indoramin, bethanidine, debrisoquine, guabenxan,  
guanadrel, guanazodine, guanethidine, guanoclor, guanoxan, alprazolam, brotizolam,  
chlordiazepoxide, clobazepam, clonazepam, clorazepate, demoxepam, diazepam,  
estazolam, flurazepam, halazepam, lorazepam, midazolam, nitrazepam, nordazepam,  
oxazepam, prazepam, quazepam, temazepam, triazolam, pharmacologically acceptable  
20 salts thereof, and combinations of any of the foregoing.

38. The method of claim 37, wherein the additional active agent is selected from  
the group consisting of alprazolam, brotizolam, chlordiazepoxide, clobazepam,  
clonazepam, clorazepate, demoxepam, diazepam, estazolam, flurazepam, halazepam,  
25 lorazepam, midazolam, nitrazepam, nordazepam, oxazepam, prazepam, quazepam,  
temazepam, triazolam, and pharmaceutically acceptable salts thereof.

39. The method of claim 37, wherein the additional active agent is selected from  
the group consisting of fluoxetine, fluvoxamine, paroxetine, sertraline, and  
30 pharmaceutically acceptable salts thereof.

40. A pharmaceutical formulation for treating premature ejaculation, comprising a rapid release formulation of a therapeutically effective amount of an antidepressant drug selected from the group consisting of tricyclic antidepressants, tetracyclic  
5 antidepressants, MAO inhibitors, azaspirone antidepressants, and atypical non-SRI antidepressants, and a pharmaceutically acceptable carrier.

41. The formulation of claim 40, wherein the antidepressant drug is selected from the group consisting of tricyclic antidepressants, tetracyclic antidepressant drugs,  
10 and combinations thereof.

42. The formulation of claim 41, wherein the antidepressant drug is selected from the group consisting of amitriptyline, amoxapine, butriptyline, clomipramine, demexiptiline, desipramine, dibenzepin, dimetacrine, dothiepin, doxepin, imipramine,  
15 iprindole, lofepramine, maprotiline, melitracen, metapramine, mianserin, mirtazapine, nortriptyline, propizepine, protriptyline, quinupramine, setiptiline, tianeptine, trimipramine, and combinations thereof.

43. The formulation of claim 42, wherein the antidepressant drug is  
20 clomipramine or an acid addition salt thereof.

44. The formulation of claim 43, wherein the antidepressant drug is clomipramine hydrochloride.

45. The formulation of claim 40, wherein the antidepressant drug is selected from the group consisting of monoamine oxidase inhibitors.  
25

46. The formulation of claim 45, wherein the antidepressant drug is selected from the group consisting of amiflamine, brofaromine, clorgyline,  $\alpha$ -ethyltryptamine,  
30 iproclozide, iproniazid, isocarboxazid, mebanazine, moclobemide, nialamide, pargyline,

00996407 "FOIA" 20190605

phenelzine, pheniprazine, pirlindole, safrazine, selegiline, tolloxatone, tranlycypromine,  
and combinations thereof.

47. The formulation of claim 40, wherein the antidepressant drug is selected from  
5 the group consisting of azaspirone antidepressants.

48. The formulation of claim 47, wherein the antidepressant drug is selected from  
the group consisting of buspirone, gepirone, ipsapirone, tandospirone, tiaspirone, and  
combinations thereof.

10 49. The formulation of claim 40, wherein the antidepressant drug is an atypical  
non-SRI antidepressant selected from the group consisting of amesergide, amineptine,  
benactyzine, bupropion, fezolamine, levoprotiline, medifoxamine, mianserin, minaprine,  
oxaflozane, oxitriptan, rolipram, teniloxazine, tofenacin, trazodone, tryptophan,  
15 viloxazine, and combinations thereof.

50. The formulation of claim 40, in unit dosage form.

51. The formulation of claim 50, wherein the antidepressant drug is present in an  
20 amount of about 0.1 mg to about to about 300 mg.

52. The formulation of claim 51, wherein the amount is in the range of about 1  
mg to about 100mg.

25 53. The formulation of claim 52, wherein the amount is in the range of about 1  
mg to about 50 mg.

54. The formulation of claim 40, in the form of a rapidly disintegrating tablet.

30 55. The formulation of claim 40, in the form of an effervescent tablet.

FILED OCT 20 2019



56. The formulation of claim 40, in the form of an open matrix network tablet.

57. A formulation of claim 40, adapted for transmucosal drug administration,  
5 wherein the carrier is suitable for transmucosal drug delivery buccally, sublingually,  
intranasally, rectally, or by inhalation.

58. The formulation of claim 57, comprising a solid dosage form for application  
to the buccal mucosa, and wherein the carrier is suitable for buccal drug delivery.

10

59. The formulation of claim 58, wherein the carrier is a hydrolyzable polymer.

60. The formulation of claim 59, wherein the dosage form further comprises an  
adhesive suitable for affixing the dosage form to the buccal mucosa.

15

61. The formulation of claim 57, comprising a dosage form for application to the  
sublingual mucosa, and wherein the carrier is suitable for sublingual drug delivery.

62. The formulation of claim 57, comprising a dosage form for application to the  
20 rectal mucosa, and the carrier is suitable for rectal drug delivery.

63. The formulation of claim 62, comprising a rectal suppository.

64. The formulation of claim 57, comprising a dosage form suitable for  
25 inhalation.

65. The formulation of claim 64, comprising a liquid.

66. The formulation of claim 64, comprising a dry powder.

30

TOPT 2049660

67. The formulation of claim 64, comprising an aerosol composition.

68. The pharmaceutical formulation of claim 40, comprising an intranasal solution.

5

69. The formulation of claim 40, in the form of a gum.

70. The formulation of claim 40, in the form of a transdermal drug delivery device adapted to be affixed to an individual's body surface.

10

71. A packaged kit for a patient to use in the treatment of premature ejaculation, comprising: a pharmaceutical formulation of an antidepressant drug selected from the group consisting of tricyclic antidepressants, tetracyclic antidepressants, MAO inhibitors, azaspirone antidepressants, and atypical non-SRI antidepressants; a container housing the pharmaceutical formulation during storage and prior to administration; and instructions for carrying out drug administration in a manner effective to treat premature ejaculation.

15

72. The packaged kit of claim 71, wherein the pharmaceutical formulation is a rapid-release dosage form containing a unit dosage of the antidepressant drug, the unit dosage being a therapeutically effective dosage for treatment of premature ejaculation.

20

00996407.1.2.101  
"PATENT"